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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
05/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,253	SAEKI ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 2/5/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Applicant's argument that claims 2-3 and 30-31 are readable on the elected species and should be rejoined is found to be persuasive upon re-consideration (see below discussion under "Election of Species").

This rejection is made final. It is noted that rejoined claims 2,3, and 30-31 would have been rejected for the same reasons as the rejected claims 1, 4, 29, and 32-34 had these claims been examined in the Office action mailed 9/12/07, under 102(b) and 103(a). Thus, the finality of the instant claims is deemed to be proper, notwithstanding the fact that claims 2, 3, and 30 and 31 were not examined in the previous Office action.

This action is made final.

Status of the Claims

Claims 1, 2, 3, 4, 29, 30, 31, 32, 33, and 34 are currently pending in this application.

Claims 1-4, and 29-34 are under examination.

Claim amendment

Applicant's amendment, received 2/5/08, is acknowledged and made of record.

Applicant statement that claims 1 and 29 have been amended to recite the term "to a subject in need thereof," while claim 1 is further amended to recite the term “treating" is acknowledged and made of record.

Applicant’s statement that no new matter is believed to have been added by the amendment is acknowledged.

Interview

Applicant’s statement memorializing the interview of October 30, 2007, is also acknowledged.

Election of Species

Applicant’s traversal arguments that election of species requirement should be withdrawn for the following summarized reasons (see applicant's Response received 2/5/08 at pages 9-10):

1) The presently recited compounds are known, as described in the specification at paragraph 0026 (US 20007/0021418);

2) Only the utility for the presently-recited compounds need to be searched, as applicant's Attorney pointed out during the interview of October 30, 2007;

3) There is no justification for an election of species with regard to the recited compounds;

4) There is no justification for an election of species with regard to a particular disease.

5) There is no undue burden in examining the presently-claimed invention, particularly as now claimed.

6) There is no justification for holding claims 2,3,30, and 31 withdrawn from consideration because these claims also read on the elected species.

In response, it is first noted that applicant's response to the election requirements, received 6/25/07, failed to indicate the claims readable on the elected species.

Upon reconsideration, claims 2, 3, 30, and 31 are rejoined as these claims are found to read on the elected species.

Applicant's traversal arguments are not found to be persuasive for the following reasons:

1) The compounds species encompassed by the instant claims are independent or distinct because they represent different chemical compounds. These different compounds have also acquired a different status in the art.

2) The disease species represent independent or distinct clinical conditions. Therapeutic agents used to treat one condition is not routinely used to treat the other conditions encompassed by the claims.

3) Based on the multiplicity of compound species and disease species encompassed by the instant application, an undue search burden will be created if all of the species were to be examined together.

The restriction/restriction requirements, mailed 5/23/07, are maintained and made final for the above reasons.

Response to applicant's arguments/remarks

Rejection under 102(b) (claims 1, 4, 29, and 32-33)

Applicant contends that this rejection should be withdrawn for the following summarized reasons (see applicant's Response, received 2/5/08, at pages 10-11):

1) Ohkuchi et al. (US Patent 6,348,468, which is the equivalent of WO 99/25697) is drawn to treating a universe of subjects in which interleukin-1β (IL-1-beta) production is implicated. There is nothing in the prior art to suggest any nexus between IL-1-beta production and OP N production.

2) The examiner relies on Ohkuchi et al. for the teaching of ischemic nephritis (col. 13, line 20), which the examiner finds is a kidney disease; claim 33 recites the term "kidney disease." However, claim 333 is limited by the requirement that the members of the disease Markush group require that it result from enhanced OPN production. Furthermore, ischemic nephritis has not been shown to result from enhanced OPN production.

3) The examiner finds that inhibiting OPN production is an inherent characteristic of the presently-recited pyridazine compounds. But the inherent property is applicant's discovery as applicant's are not claiming the compounds (see Response, page 11, lines 4-6).

In response, the rejection is maintained as applicant's arguments are not found to be persuasive for the reasons made of record in the Office action, mailed 9/12/07, at pages 3-6 and for the additional reasons

a) Claim 1 “[a] method of inhibiting osteopontin (OPN) production, comprising administering to a subject in need thereof an effective amount of a pyridazine derivative ...," which is directed to a mechanism of action of said compounds. The recitation of the term "administering to a subject in need thereof" does not in this case give life to the claimed underline mechanism of inhibiting osteopontin. To the extent that applicant's discovery is the discovering of a new mechanism of action for a known group of compounds, coupled with the fact that a compound's function is not separable from actual compound, the claimed underlined mechanism of action of the compounds encompassed by the instant claims is deemed to an inherent characteristic of the instant claimed methods.

b) Applicant’s above arguments fail to reasonably address the specifically recited claimed limitations.

Rejection under 103(a)

Applicant contends that this rejection should be withdrawn for essentially the following summarized reasons:

1) The above arguments set forth in response to the rejection under 102(b) are incorporated by reference.

2) McPhaden et al. do not remedy the deficiencies of Ohkuchi et al. as McPhaden simply discloses a connection between OPN production and multiple myeloma. However, applicant’s do not profess to be the first to recognize this connection. Rather, applicant has discovered that certain compounds inhibit the production of OPN, and thus are useful for treating multiple myeloma. Neither

McPhaden et al. nor any other prior art discloses any connection or nexus between inhibiting IL-1-beta, as disclosed by Ohkuchi et al, and inhibiting OPN production.

In response, the rejection is maintained for the reasons made of record in the Office action, mailed 9/12/07, at pages 6-7, and for the additional reasons set forth above in the response to the rejection under 102(a).

Rejection under 112, 2nd para

This rejection is withdrawn in view of applicant's amendment.

Nonstatutory obviousness-type double patenting (ODP) rejections

Applicant contends that the provisional ODP rejection should be withdrawn for the following reasons;

1) Applicant disagrees with the examiner's position that the term "prevention … of rheumatoid arthritis in a subject" reasonably encompasses treatment of subjects with or without arthritis i.e. multiple myeloma. However, the examiner cites no evidence to support the connection between prevention of rheumatoid arthritis and inhibiting ONP production.

In response, the rejection is maintained as applicant's arguments are not found to be persuasive for the reasons made of record in the Office action, mailed 9/12/07, at pages 9-10).

REJECTIONS

Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, and 29-34 are rejected under 35 USC 102(b) as being anticipated by Ohkuchi et al. (US Patent 6,348,468).

The rejection made of record in the Office action mailed 9/27/07 at pages 3-6 is incorporated by reference.

To reiterate, Ohkuchi et al. teach applicant's elected compound species and methods of treatment comprising administering said compound, wherein said compounds are effective (see Example 132, col. 54; and abstract). Reference claim 7 recites the term "[a] pharmaceutical composition for inhibiting interleukin-1.beta. production in a mammal, comprising: a) one or more of the compound of claim 1, or salt thereof, in an amount effective to effect said inhibition; …," which satisfies the limitation "administering to a subject in need thereof an effective amount of a pyridazine derivative …" as recited in claim 1, for example, because administration of an effective amount to inhibit IL-1 beta would necessarily also inhibit OPN production in the absence of evidence to the contrary. Ohkuchi et al. teach that compounds having the above referenced formula are effective ingredients when administered orally or parenterally to an adult in an amount of about 0.01 to 1,000 mg per day (col. 13, lines 39-45)i this reference teaching is construed to be the functional equivalent of the following term recited in instant claims 1 and 29:

"administering an effective amount of a pyridazine derivative …" The term "[a]

therapeutic method of treating a disease resulting from enhanced OPN production," given it broadest reasonable possible interpretation is construed to overlap with the teaching of Ohkuchi et al. of *ischemic nephritis* (col. 13, lines 10-23), which is reasonably construed to exemplify the term *"a kidney disease,"* as recited in instant claim 33. Also, reference claim 9 is directed to treating a human patient suffering from arthritis. Thus, the treatment group taught by Ohkuchi et al. overlaps with the targeted population encompassed by the instant claims as evidenced by the teaching of Ashkar et al. (WO 00/63241) that use of early T lymphocyte activation-1/osteopontin modulators for modulating a type-1 immune response in humans for treating cancer, AIDS, allergy, bacterial arthritis, granulomatous disorder, and glomerulonephritis (abstract only).

Rejoined claims 2-3 and 30-31 overlap with the compounds taught by Ohkuchi et al. because the elected compound species reads on these claims as further evidenced by applicant's admission that the instant claimed compounds are taught by Ohkuchi et al., and are already known in the art, is also acknowledged.

To the extent that the instant claims recite as the only active step the "administering to a subject in need thereof an effective amount of a pyridazine compound of formula I as recited in claim 1, coupled with the fact that the reference population and the instance claimed population overlaps and the fact that the function of a compound is not severable from the compound itself, the contemplated effect to be achieved in practicing the instant claimed methods is found to be an inherent characteristic of the claimed method.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 34 are rejected under 103(a) as being unpatentable over Ohkuchi et al. (US Patent 6,348,468), in view of McPhadden et al. (Plasma osteopontin levels in multiple myeloma. Blood. 1994;84(10, Suppl 1), page 177a, abstract #674).

The rejection made of record in the Office action mailed 9/27/07 at pages 6-7 is incorporated by reference.

The above discussion of Ohkuchi et al. is incorporated by reference. Ohkuchi et al. do not teach multiple myeloma as recited in instant claim 34.

McPhadden et al. is added to show the general state of the art regarding multiple myeloma. McPhaden et al. teach osteopontin (OPN) appears to be important in bone

metabolism and may be a clinical marker of osteoblast and/or osteoclast activity in multiple myeloma (abstract). McPhaden et al. also teach that a number of osteoclast activating factors have been implicated in multiple myeloma including interleukin-1/3 (IL-l-beta).

Based on the teaching of McPhaden et al. that osteopontin appears to be important in bone metabolism, someone of skill in the art would have been motivated to combine the teachings of Ohkuchi et al. and McPhaden et al. to create the instant inventive concept. Thus, someone of skill in the art at the time the instant claimed invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Thus, claims 34 is found to be obvious in view of the above cited art.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, and 29-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-9 of copending appl. 11/574,319 and claims for the reasons delineated in the Office action of 9/27/07 at pages 9-10. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

Relevant Art of Record

The below art references made of record and relied upon is considered pertinent to applicant's invention.

Chabas et al. (US Patent Application Publication No. 2005/0119204 A1)teach a methods for inhibiting the onset of, and treating, osteopontin-related disorders, as well as compositions for practicing the same (page 9, para.0137 to page 16, para. 0191; see also abstract).

Ashkar et al. (WO 00/63241) teach use of early T lymphocyte activation-1/osteopontin modulators for modulating a type-1 immune response in humans for treating cancer, AIDS, allergy, bacterial arthritis, granulomatous disorder, and glomerulonephritis (abstract only).

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

25 April 2008

/C. R./

Examiner, Art Unit 1611

/Raymond J Henley III/
Primary Examiner, Art Unit 1614